MODIFIED GRIFFITHSIN TANDEMERS FOR ENHANCED ACTIVITY AND REDUCED VIRAL AGGREGATION

SUMMARY

NCI seeks partners to commercialize Griffithsin and Griffithsin tandemers as therapeutics for HIV infections that are resistant to native GRFT, specifically, additional studies on stability, toxicity, immunogenicity, and large-scale production.

REFERENCE NUMBER

E-034-2013

PRODUCT TYPE

- Therapeutics

KEYWORDS

- mGRFT tandemers
- antiviral

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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DESCRIPTION OF TECHNOLOGY

Griffithsin (GRFT) is a lectin with potent antiviral properties that is capable of preventing and treating infections caused by a number of enveloped viruses (including HIV, SARS, HCV, HSV, and Japanese encephalitis) and is currently in clinical development as an anti-HIV microbicide. In addition to its broad antiviral activity, GRFT is stable at high temperature and at a broad pH range, displays low toxicity and immunogenicity, and is amenable to large-scale manufacturing. Native GRFT is a domain-swapped homodimer that binds to viral envelope glycoproteins and has displayed mid-picomolar activity in cell-based anti-HIV assays.

Researchers at NCI's Molecular Targets Lab developed synthetic proteins that comprise two (or more) obligate monomers (“mGRFT”) joined by an amino acid linker to form tandemers (“mGRFT tandemers”). Each obligate monomer is generated by the addition of Gly-Ser residues in the hinge region of wild-type

GRFT. Two or more obligate monomers are joined by an amino acid linker to form the mGRFT tandamers. The properties of the mGRFT tandemers can be modulated by the length of the amino acid linker and the number of obligate monomers co-joined. mGRFT tandemers exhibit gore potent anti-viral properties when compared against native GRFT and are equipotent against viruses that are both sensitive and resistant to naive GRFT. As such, potential uses of the invention tandemers include topical and intravenous therapy to treat HIV infection, particularly to treat HIV infections that are resistant to native GRFT.

POTENTIAL COMMERCIAL APPLICATIONS

- Broad-spectrum antiviral agent similar to wild type GRFT
- Potential activity against SARS CoV, MERS, Ebola, HCV and influenza

COMPETITIVE ADVANTAGES

- Broad antiviral activity and stable at high temperature and at a broad pH range
- Displays low toxicity and immunogenicity

INVENTOR(S)

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DEVELOPMENT STAGE

- Pre-clinical (in vivo)

PUBLICATIONS

- Moulaei T. et al., Griffithsin tandemers: flexible and potent lectin inhibitors of the human immunodeficiency virus. Retrovirology. 2015 Jan 23;12:6; A. Chatterjee et al.,Griffithsin and Carrageenan Combination To Target Herpes Simplex Virus 2 and Human Papillomavirus, Antimicrob Agents Chemother. 2015 Dec; 59(12): 7290–7298.

PATENT STATUS

- **U.S. Filed:** PCT Application No. PCT/US2014/04099 filed June 5, 2013

THERAPEUTIC AREA

- Infectious Diseases